REMARKS

Status of the Claims

Claims 1-23 are pending and claims 1-7 are under consideration in this application, claims 8-13 having been withdrawn from consideration for allegedly been drawn to different inventions. All the claims under consideration stand rejected.

Claim 1 has been amended and the amendments to it are supported by the specification, e.g., at page 3, lines 16-18, page 5, line 13, page 5, lines 18-20, page 7, lines 29-31, page 8, lines 6-26, and page 11, lines 27-31. Claims 3-7 have been amended to conform them to the language of amended claim 1 and in the interest of enhanced clarity. Claims 2 and 9 -11 have been cancelled and new claims 24-27 have been added. Claims 24-26 are supported by the specification, e.g., at page 8, lines 6-8, page 8, lines 17-26, page 11, lines 27-29, and page 18, lines 15-23. Claim 27 is supported by the specification, e.g., at page 7, lines 3-7.

In order to retain the right under 37 C.F.R. § 1.121 to rejoin claims directed to methods of using the presently claimed polypeptides once the present claims have been held allowable, appropriate method of use claims have been amended herein to conform them to the scope of the polypeptide claims presently under consideration. "Method of use" claims that have been so amended include claims 12-17.

None of the amendments made herein or the new claims add new matter.

After entry of the amendments made herein, claims 1 and 3-8, and 12-27 will be pending and claims 1, 3-7, and 24-27 will be under consideration in this application, claim 2 and 9-11 having been cancelled and claims 24-27 having been added.

Objection to disclosure

Applicants have in the above amendment to the specification deleted the hyperlinks on page 6, lines 4 and 5, of the specification. Applicants respectfully submit that this amendment renders moot the objection to the disclosure on page 2, lines 12-15, of the Office Action.

35 U.S.C. § 112, second paragraph, rejections

Claims 1-7 stand rejected as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter that Applicants regard as the invention.

From the comments on page 3, lines 7-13, of the Office Action, Applicants understand the Examiner's position to be that it is unclear what molecule the term "B7-H2" refers to. Applicants disagree with this position. Thus, for example, from the text on page 23, lines 2-7, of the specification, it is clear what human polypeptide is covered by the term "B7-H2" as used in the instant application (i.e., the polypeptide whose sequence is depicted in Wang et al. Blood 96:2808-2813, 2000). Moreover, from the same text of the specification, it is clear that both human and mouse polypeptides covered by the term "B7-H2" are the same as those described and depicted as B7RP-1 in Yoshinaga et al., Int. Immunol. 12:1439-1447, 2000.

In light of these citations in the text of the instant specification, Applicants respectfully submit that it is perfectly clear exactly what molecules are referred to by the term "B7-H2" in the instant application and therefore request that the rejection under 35 U.S.C. § 112, second paragraph, be withdrawn.

35 U.S.C. § 112, first paragraph rejections

(a) Claims 1-3, 5, and 7 stand rejected on the grounds that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

From the comments on page 4, line 1, to page 7, line 5, of the Office Action, Applicants understand the Examiner's position to be that it would involve excessive experimentation for one of skill in the art to establish what polypeptides (homologous variants and fragments of ICOS) would be covered by the instant claims. Applicants respectfully disagree with this position.

First, Applicants point out that it is not required that the specification teach how to make and use every polypeptide covered by the instant claims, only a reasonable number. Moreover, the amount of experimentation to determine such a reasonable number of polypeptides is not determinative of enablement. It is whether such experimentation, given the teaching of the

specification and the knowledge and skill of those in art, would be of a routine nature. The Examiner is reminded that the knowledge and skill of practitioners in the art (e.g., biochemists, molecular biologists, and cell biologists) are extraodinarily high.

Applicants respectfully submit that in view of the teachings of the instant specification as to where critical residues in the ICOS lie (see Examples 2 and 3 on pages 23-27 of the specification), one of skill in the art would be able to design a large number of polypeptides of various sizes and containing various mutations that would have a good chance of performing as required by the claims. Having designed and made such polypeptides, such an artisan would know, based on both the teachings of the specification (e.g., Examples 1-3) and his/her own knowledge and skill how to identify those indeed having the requisite function.

Despite these considerations, in order to expedite prosecution of the instant application, Applicants have greatly reduced the range of polypeptides covered by the claims and hence also, although not required by the law, the amount of routine experimentation necessary to obtain a reasonable number of polypeptides falling within the scope of the claims. Thus, independent claim 1 now requires that ICOS-derived variants be derived from the extracellular domains of wild-type ICOS, that the relevant ICOS extracellular domains be those of SEQ ID NO:9 or SEQ ID NO:10, that the variants contain one or more amino acid substitutions, that the variants be at least 80% identical to the relevant ICOS molecules, and that ICOS-derived fragment variants be at least 8 amino acids in length. These amendments to claim 1 greatly reduce the amount of routine experimentation one skilled in the art would need to carry out in order to obtain a reasonable number of polypeptides falling within the scope of the claims.

(b) Claims 1-7 stand rejected on the grounds that the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

From the comments on page 7, line 6, to page 8, line 4, of the Office Action, Applicants understand the Examiner's position to be that, in view of the word "having" in claim 1: (a) wild-type ICOS molecules can be any of a wide range of undefined molecules other than that SEQ ID

NO:12; and (b) the claimed polypeptides can contain undisclosed sequence(s) on either end of the ICOS-derived sequences.

Applicants have deleted the word "having" and, with respect to item (a) above, have limited the regions of ICOS and the ICOS molecules from which the ICOS variants are derived to the extracellular domains of human and mouse ICOS (i.e., SEQ ID NOs: 10 and 9, respectively).

With respect to item (b) above, Applicants have added an alternative embodiment to claim 1 explicitly allowing for non-ICOS-derived sequences on either or both ends of the variant ICOS sequence. Thus, this alternative embodiment essentially specifies a fusion protein comprised of an ICOS-derived portion and a heterologous (non-ICOS-derived) portion. Claims specifying fusion proteins in which heterologous sequences are undefined are routinely allowed by the U.S. Patent and Trademark Office. The specification provides examples of a variety of possible non-ICOS sequences that could be used and new dependent claims 24-26 specify these. Applicants point out that it would take no more than routine experimentation to determine whether a particular non-ICOS sequence of interest added to an ICOS-derived variant of interest affects the function of the variant. Moreover, as it now reads, claim 1 only requires that that ICOS-derived variant part of the polypeptide have the requisite B7-H2-binding ability. At least some of appropriate non-ICOS sequences (e.g., tags that facilitate purification of recombinant molecules; see, for example, page 8, lines 17-26, of the specification) can be removed prior to use. In addition, where an appropriate tag sequence allows for detection of the relevant fusion polypeptide, the fusion polypeptide need not always have B7-H2-binding ability. Thus it is not always required that the combination of ICOS-derived and unrelated sequence have the requisite function.

In light of the above considerations, Applicants respectfully request that the rejections under 35 U.S.C. § 112, first paragraph, be withdrawn.

35 U.S.C. §§ 102(b) and 102(e) rejections

(a) Claims 1, 2, and 7 stand rejected as allegedly being anticipated by U.S. Patent No. 6,521,749 (the '749 patent).

In that the '749 patent was published on February 18, 2003, and the instant application was filed on February 7, 2002, Applicants respectfully submit that the '749 patent is not "102(b)" prior art with respect to the present application.

Even if the '749 patent is prior art with respect to the instant application, Applicants respectfully submit that it neither directly or inherently anticipates the instant claims.

First, instant claim 1 requires that the ICOS-derived portion of the polypeptide contain one or more amino acid substitutions compared to the corresponding wild-type ICOS sequence. The ICOS-derived portion of the fusion protein described by the '749 patent apparently contains no amino acid substitutions relative to the corresponding part of the full-length, wild-type ICOS molecule. Moreover, instant claim 1 requires that ICOS-derived variant part of the claimed polypeptide have altered affinity for B7-H2 relative to the corresponding part of wild-type ICOS. Since the ICOS-derived part of the molecule described by the '749 patent is identical to the corresponding part of the wild-type polypeptide, it cannot have altered affinity for B7-H2 compared to the corresponding part of the wild-type peptide. Moreover, Applicants point out that, while the whole ICOS-fragment-containing fusion protein described in the '749 patent could have altered affinity for B7-H2 relative to wild-type ICOS (or to the wild-type ICOS fragment), it certainly would not necessarily have such altered affinity.

(b) Claims 1 and 7 stand rejected as allegedly being anticipated by U.S. Patent Application Publication No. 2002/0156242 (the '242 application).

Applicants respectfully point out that, while the sequence used for alignment with the SEQ ID NO:2 of the '242 application contains a "Q" residue at position 76, SEQ ID NO:12 as disclosed in the Sequence Listing of the instant application contains, like SEQ ID NO:2 of the '242 application, a "S" residue at position 76.

The '242 patent neither directly nor inherently anticipates the instant claims.

First, instant claim 1 requires that the variant ICOS polypeptide (or the variant ICOS-derived portion of the polypeptide) contain one or more amino acid substitutions compared to the corresponding portion of the wild-type ICOS polypeptide. No specific substitutions of the ICOS polypeptide (or of ICOS-derived portions of fusion proteins) are mentioned in the '242 application. In addition, instant claim 1 requires that the claimed variant ICOS-derived polypeptide (or variant ICOS-derived part of the claimed polypeptide) have altered affinity for B7-H2 relative to the corresponding wild-type ICOS-derived polypeptide. The '242 application makes no mention at all of B7-H2, let alone requiring that the substituted ICOS molecules it mentions have altered affinity for B7-H2. Moreover, it is certainly not necessarily the case that any of the unspecifically described substitutions mentioned in the '242 application (in, for example, paragraphs 0154, 0159, and 0160) would have resulted in altered affinity for B7-H2 as required by the instant claims. In fact, in its description of variant polypeptides, the '242 application states that such molecules have "substantially the same biological properties as the polypeptide having the amino acid sequence shown in Sequence Listing" (paragraph 0154) and that mutants "can be screened for biological activity to identify mutants that retain activity" (paragraph 0159).

In light of the above considerations, Applicants respectfully request that the rejections under 35 U.S.C. § 102 be withdrawn.

CONCLUSIONS

Applicants submit that the claims under consideration are in condition for allowance, which action is requested.

If the Examiner would like to discuss any of the issues raised in the Amendment, Applicants' undersigned representative can be reached at the telephone number listed below.

Applicants submit herewith a request for an automatic extension of time and a check in payment of the extension of time. Please charge any other fees or make any credits to Deposit Account No. 06-1050, referencing Attorney Docket No. 07039-331001.

Respectfully submitted,

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Stuart Macphail, Ph.D., J.D.
Reg. No. 44,217

Fish & Richardson P.C.
Citigroup Center
52nd Floor
153 East 53rd Street
New York, New York 10022-4611
Telephone: (212) 765-5070
Facsimile: (212) 258-2291

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